

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2004/009675

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl⁷ A61K45/00, 31/195, 33/00, A61P9/08, 9/00, 9/10, 25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl⁷ A61K45/00, 31/195, 33/00, A61P9/08, 9/00, 9/10, 25/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho 1922-1996 Toroku Jitsuyo Shinan Koho 1994-2004

Kokai Jitsuyo Shinan Koho 1971-2004 Jitsuyo Shinan Toroku Koho 1996-2004

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS (STN), MEDLINE (STN), BIOSIS (STN), REGISTRY (STN), EMBASE (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JAGGER, Justin E. et al., Role of erythrocyte in regulating local O ₂ delivery mediated by hemoglobin oxygenation, Am. J. Physiol. Heart Circ. Physiol., 2001, Vol.280, pages H2833 to H2839, full text, particularly, page H2833, Abstract, Figs. 2, 3	1-7, 10-15, 34
X	Yasunobu HIRATA, "Koketsuatsu to NO", Igaku no Ayumi, 2003, Vol.204, No.9, pages 607 to 610, full text, particularly, page 607, Abstract	1-7
X	FULLERTON, Davis A. et al., Adenosine is a selective pulmonary vasodilator in cardiac surgical patients, CHEST, 1996, Vol.109, pages 41 to 46, full text, particularly, page 41, Abstract	1-7

☒ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
24 September, 2004 (24.09.04)Date of mailing of the international search report
12 October, 2004 (12.10.04)Name and mailing address of the ISA/
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DIJI, A et al., The local effect of carbon dioxide on human blood vessels, Am. Heart J., 1960, Vol.60, pages 907 to 914, full text, particularly, page 907	1-7
X	AGRAWAL B. et al., Acute effects of bezafibrate on blood pressure and renal haemodynamics in SHR and WKY rats, Nephrol. Dial. Transplant, 1998, Vol.13, pages 333 to 339, full text, particularly, page 333, Abstract	1-7
X	SPRAGUE, Randy S. et al., Deformation-induced ATP release from red blood cells requires CFTR activity, American Journal of Physiology, 1998, Vol.275, pages H1726 to H1732, full text, particularly, page H1726, Abstract	10-15, 41-43
X	KOZMA, Fruzsina et al., Contribution of endogenous carbon monoxide to redulation of diameter in resistance vessels, Am.J. Physiol., 1999, Vol.276, pages R1087 to 1094, full text, particularly, page R1087, Abstract	10-16
X	LANDRY, Donald W. et al., The ATP-sensitive K ⁺ channel mediates hypotension in endotoxemia and hypoxic lactic acidosis in dog, J.Clin.Invest. 1992, Vol.89, pages 2071 to 2074, full text, particularly, page 2071, Abstract	10-16, 41-43
X	JP 2001-507375 A (Takashi YONETANI), 05 June, 2001 (05.06.01), Full text; particularly, Claims 1 to 21; example 4 & WO 99/01146 A1	19-21, 25
X	JP 6-16693 A (Research Institute For Production Development), 25 January, 1994 (25.01.94), Full text; particularly, Claims 1 to 5 (Family: none)	22-24, 31
X	JP 11-512436 A (DUKE UNIVERSITY MEDICAL CENTER), 26 October, 1999 (26.10.99), Full text; particularly, Claims 30, 31 & WO 97/10265 A1	25-29
A	WO 03/000244 A1 (AVENTIS PHARMA DEUSCHLAND GMBH.), 03 January, 2003 (03.01.03), Full text; particularly, Claims 1 to 8 & US 2003/083385 A1	31-33

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 8, 9, 17, 18, 35-40
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 8, 9, 17, 18 and 35 to 40 pertain to methods for treatment of the human body by therapy.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See extra sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

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Continuation of Box No.III of continuation of first sheet (2)

With respect to claims 4-6:

Considering that the invention of claim 1 of this application "promoter of ATP release from red blood cells, comprising a substance capable of stabilizing the structure of hemoglobin in red blood cells in its T-state" is the specified invention, it appears that the matter common with the invention of claim 4 "pharmaceutical composition comprising a substance capable of stabilizing the structure of hemoglobin in red blood cells in its T-state" is "pharmaceutical composition comprising a substance capable of stabilizing the structure of hemoglobin in red blood cells in its T-state". However, since medical drugs capable of promoting ATP release from red blood cells, comprising carbon dioxide as an active ingredient are publicly known as described in the following literature, it does not appear that in view of comparison with the prior art, the novel main features of the two inventions are identical with each other.

Further, it does not appear that the two inventions possess common technical task having been left unresolved until the filing date of this application.

Therefore, the invention of claims 4-6 of this application does not constitute with the invention of claim 1-3 and 7 a group of inventions linked with each other so as to form a single general inventive concept.

With respect to claims 10-16:

It appears that the matter common to the invention of claim 10 of this application "inhibitor of ATP release from red blood cells, comprising a substance capable of stabilizing the structure of hemoglobin in red blood cells in its R-state" and the above specified invention is "controlling of ATP release through stabilization of the structure of hemoglobin in red blood cells". However, as mentioned above, this feature is publicly known.

Therefore, for the similar reason, the invention of claims 10-16 of this application does not constitute with the invention of claims 1-3 and 7 a group of inventions linked with each other so as to form a single general inventive concept.

With respect to claims 19-33:

It appears that the invention of claim 19 of this application "red blood cells wherein the structure of hemoglobin has been stabilized in its T-state" and the invention of claims 25-33 "pharmaceutical composition comprising such red blood cells" is common to the above specified invention in "stabilizing the structure of hemoglobin in red blood cells in its T-state". However, as mentioned above, this feature is publicly known. Therefore, for the similar reason, the invention of claims 19-33 of this application does not constitute with the invention of claims 1-3 and 7 a group of inventions linked with each other so as to form a single general inventive concept.

The same applies claims 22-24.

With respect to claims 34-38:

With respect to the invention of claim 34 of this application "method of ATP assay characterized by carrying out quantitative determination of ATP released from red blood cells with dependence on oxygen concentration", because of no limitation to use of an ATP release promoter according to the specified invention, it does not appear that the novel main features of this invention and the above specified invention are identical with each other. Further, it does not appear that the two

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Continuation of Box No.III of continuation of first sheet (2)

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inventions possess common technical task having been left unresolved until the filing date of this application.

Therefore, the invention of claims 34-38 of this application does not constitute with the invention of claim 1-3 and 7 a group of inventions linked with each other so as to form a single general inventive concept.

With respect to claims 41-43:

Because the contained active ingredients are different from each other, it appears that the invention of claim 41 of this application and the above specified invention are common to each other only in the use "controlling of ATP release from red blood cells". However, as mentioned above, this use is publicly known.

Therefore, as studied above, the invention of claims 41-43 of this application does not constitute with the invention of claim 1-3 and 7 a group of inventions linked with each other so as to form a single general inventive concept.

Reference: JAGGER, Justin E. et al, Role of erythrocyte in regulating local O₂ delivery mediated by hemoglobin oxygenation, Am. J. Physiol. Heart Circ. Physiol., 2001, Vol.280, ppH2833-2839